TREATMENT OF FEMALE SEXUAL DYSFUNCTION

The present invention relates to the treatment of female sexual dysfunction and is directed particularly, but not exclusively, to Hypoactive Sexual Desire Disorder.

The term female sexual dysfunction is a term used for various disorders of the sexual process in women and is categorised by pain associated with intercourse or by a disturbance in the process that forms the sexual response cycle. The sexual response cycle is divided into four distinct phases consisting of (i) the desire phase; (ii) the arousal or excitement phase; (iii) the orgasmic or plateau phase; and (iv) the resolution phase.

The (i) desire phase involves fantasies about and the desire to have sexual activity. The lack of such fantasies and desires and the general lack of receptivity to sexual activity is referred to as Hypoactive Sexual Desire Disorder (HSDD). This disorder may cause personal distress or interpersonal difficulties.

The (ii) arousal or excitement phase is typically evidenced by vaginal lubrication as a consequence of increased fluid production through blood flow. Dysfunction in this cycle is termed Sexual Arousal Disorder and manifests itself as an inability to obtain or maintain sufficient and adequate vaginal lubrication or a swelling response during this phase. This disorder is commonly associated with post-menopausal women and may cause extreme personal distress and interpersonal difficulties. That said, all women may be affected by this disorder at some stage in their lives.

The final phase, (iv) the resolution phase, is when the blood flow returns to normal and muscle tension and tightness dramatically decrease.

There are further forms of sexual dysfunction, such as female orgasmic disorder which is described as a persistent or recurrent delay or absence of an orgasm following the normal sexual excitement phase. This disorder may be present in women as a result of surgery or hormone deficiencies and/or present in women who have never achieved an orgasm.

Additionally, there are sexual pain disorders and these generally fall into one of two categories. The first category is dyspareunia and concerns genital pain associated with sexual intercourse. Pain can be associated with initial penetration or during deep thrusting, resulting in an intensity of pain which makes the prolonging of intercourse near impossible. The other category of sexual pain disorder is vaginismus and this is defined as the recurrence or persistent involuntary spasm or contraction of the perineal muscles that surround the outer third of the vagina when the insertion of any object is attempted.

The female sexual dysfunction which is of principal concern to the present invention is the treatment of Hypoactive Sexual Desire Disorder (HSDD). Of all female sexual problems, a lack of interest in sexual activity is most prevalent, affecting 30% of women.[1]

HSDD concerns sexual desire and this desire has two main manifestations - "proceptivity" (seek out and/or initiate sexual activity) and "receptivity" (accept sexual activity when offered). These manifestations are analogous to an appetite for food, the analogy being that when we feel hungry we seek out food, or when we do not feel hungry we do not seek out food until we see it tasteful and attractively presented. For many women, the complaint of lack of sexual desire is found, typically, to mean a lack of proceptivity, the woman maintaining receptive sexual behaviour.

Indeed the "appetite" phase of sexual functioning can be conceptualised in two components - designated "sexual drive" and "sexual desire".[2] In this dichotomisation, the term "sexual drive" means the biological drive that generates proceptivity and receptivity. This drive is omnipotent in that it can be satisfied by a variety of behaviour (e.g. sexual activity with a partner, masturbation, sexual fantasies). Conversely, the term "sexual desire" is used to mean a desire for a specific behaviour. In effect, "sexual desire" is focused sexual drive.

It will be appreciated that the physiology of sexual drive in women is not well understood. Sexual drive is thought to be generated in specific nuclei of the hypothalamus, often called

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[1] Laumann EO, Paik A, Rosen RC. Sexual dysfunction in the United States. *JAMA* 1999; 281: 537-544.

[2] Riley A. Problems of the sexual response cycle. *The Diplomate, The Journal of the Diplomats of the Royal College of Obstetricians and Gynascologists,* 1997; 4: 270-275.

collectively the "sex drive centre". These nuclei have positive (sexually enhanced) and negative (sexually inhibiting) influences from other centres of the central nervous system mediated through neurotransmitters and neurohormones.

Treatment of HSDD may be two fold. Firstly and importantly, a correct diagnosis of HSDD would need to be made. Once a physician is comfortable that there is no organic cause and that any severe medical conditions, such as diabetes or heart disease, were correctly treated, it would then be necessary to discuss interpersonal difficulty with a partner. Once HSDD is diagnosed, the condition would be amiable to treatment with sexual therapy. A further treatment may be by hormone therapy.

Oestrogen therapy is commonly used in the pharmacological treatment of sexual dysfunction in women. Oestrogen-based therapies are generally used to increase mucus production, to provide vasodilatory effects, or to increase the general health of the vagina.[3] In such treatments, oestrogen is administered orally, by injection or topically. With oral administration, the oestrogen concentration encountered by the liver is generally four to five times greater than the oestrogen levels in peripheral blood. This effect may lead to an undesirable increase in the production of certain coagulation factors and renin substrates in the liver. Oestrogen administered by injection avoids this effect in the liver. However, all oestrogen-based therapies are known to increase the risk of endometrial hyperplasia, endometrial cancer and breast cancer in treated individuals. Due to the increased risk of endometrial hyperplasia and endometrial cancer encountered with oestrogen therapies, the use of oestrogen/progestogen combinations have been utilised. However, these have the common side effects of inducing uterine bleeding and the continuation of menstrual periods.

Alternatively, male hormones collectively known as androgens, such as testosterone, and the lack of these in the female body have been linked to forms of sexual dysfunction. Testosterone is produced in a woman's body and the pinnacle of production is generally around the woman's reproductive years. This production can wane for a variety of reasons

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[3] Nadelson et al., eds., *Treatment Inverventions in Human Sexuality* (New York: Plenum Press, 1983)

and this waning can be counter-acted in certain instances by testosterone replacement therapy. In certain cases this counter-acting effect has prompted an increase in sex drive.

Nevertheless, testosterone replacement therapy carries with it several dangers analogous to oestrogen replacement therapy and as such is far from satisfactory.

Accordingly, it is a general aim of the present invention to provide a treatment for female sexual dysfunction and delivery method for said treatment, and specifically the treatment of HSDD, which overcomes or ameliorates the problems and drawbacks associated with the prior art as well as, preferably, overcoming other apparent problems and drawbacks with medicaments for female sexual dysfunction in general.

According to a first aspect of the present invention, there is provided an aroma in the form of at least one dopamine mimetic odorant wherein said odorant(s) is capable of causing a physiological effect in, or from, the human brain which causes the amelioration of female sexual dysfunction, and particularly the amelioration of HSDD.

The use of an aroma is advantageous since it is capable of acting directly on the brain without having to pass through the blood brain barrier, this is in stark contrast to medicaments which are typically administered by ingestion or intravenously.

The dopamine mimetic ordorants (DMO) of the present invention are designed such that they can be sensed by a patient's olfactory system and act as a stimuli, or binder, to the patient's receptor proteins in the olfactory tract of the patient's brain to cause the amelioration of female sexual dysfunction, and particularly the amelioration of HSDD.

Whilst the exact mechanism is far from clear, it is suspected that DMOs of the present invention act in such a way as to initiate a chain of co-ordinated events in the brain which ultimately lead to changes in the patient's levels of dopamine and, consequently, the required amelioration. However, it is to be understood that the DMOs of the present invention may be working quite differently than has been hypothesised and that the amelioration is achieved by means other than changing a patient's level of dopamine in the brain.

It is to be understood that the use of the word dopamine here is intended to include other related neurotransmitters such as epinephrine, norpinephrine and the like.

The DMOs of the present invention are provided in a form capable of being sensed to a patient's olfactory system and comprises at least one of the following groups of compounds: steroid odorants; amines and related molecules; heterocyclic aroma molecules, including Jasmin oil; aromatic molecular mimics of the central neurotransmitter dopamine; carboxylic acids including those which may occur in trace levels in human secretions; aldehydes, including those which form trace ingredients in odorous human secretions.

Preferably, the DMOs of the present invention comprise at least one of the following recognized classes of perfume odorants: – vanilla like – (prototypical example – vanillin); carnation like – (prototypical example – isoeugenol); musk like – (prototypical example – 6,7-dihydro-1,1,2,3,3-pentamethyl-4(5H)-indanone)

Most preferably, the DMOs of the present invention comprise at least one of the following groups of compounds: vanillin; isoeugenol and a compound in the musk category, preferably the woody musk category.

Ideally, the DMOs of the present invention comprise at least one of the following: ethyl vanillin (3-ethoxy-4-hydroxybenzaldehyde); isoeugenol (2-methodoxy-4-(1-propenyl) phenol; the woody musk 6,7-dihydro-1,1,2,3,3-pentamethyl-4(5H)-indanone.

Desirably said carboxylic acids exhibit paradoxical aroma profiles, wherein these profiles combine reassuring odour notes of warm human flesh but wherein said odour notes are embedded in distinctly fruity odour notes, these odour notes can often serve to prevent the conscious mind apprehending the occult, erogenic odour note. Furthermore said aldehydes may additionally comprise new synthetic aldehydes which can exhibit a floral odour note with a heart of erogenicity.

According to a second aspect of the present invention, there is provided a range of compound(s) in the form of at least one dopamine mimetic odorant, wherein said odorant(s) is capable of causing a physiological effect in, or from, the human brain which causes the amelioration of female sexual dysfunction, and particularly ameliorate the effects of HSDD.

According to a third aspect of the present invention, there is provided a medicament comprising a range of compounds including at least one dopamine mimetic odorant wherein said odorant(s) is capable of causing a physiological effect in, or from, the human brain which causes the amelioration of female sexual dysfunction, and particularly the amelioration of HSDD.

According to a fourth aspect of the present invention, there is provided a set of formulations comprising at least one dopamine mimetic odorant, wherein said odorant(s) is capable of effecting a physiological effect in, or from, the human brain which causes the amelioration of female sexual dysfunction, and particularly the amelioration of HSDD.

According to a fifth aspect of the present invention, there is provided a medicament comprising a set of target formulations wherein said formulations include at least one dopamine mimetic odorant and said odorant(s) is capable of effecting a physiological effect in, or from, the human brain which causes the amelioration of female sexual disorder, and particularly the amelioration of HSDD.

According to a sixth aspect of the present invention, there is provided a medicament for application to a patient in avoidance of the human blood brain barrier, wherein said medicament comprises at least one dopamine mimetic odorant and said odorant(s) is capable of effecting a physiological effect in or from the human brain which causes the amelioration of female sexual disorder, and particularly the amelioration of HSDD.

According to a seventh aspect of the present invention, there is provided a compound or compounds possessing at least one dopamine mimetic odorant wherein said odorant(s) has an appropriate molecular size and electrical charge to interact with a neuroreceptor in the human brain in such a way as to have an agonistic effect in order to cause the emission of neurotransmitters which cause an effect to the central nervous system, said effect being a physiological effect which causes the amelioration of female sexual disorder, and particularly the amelioration of HSDD.

According to an eighth aspect of the present invention, there is provided a formulation or formulations possessing at least one dopamine mimetic odorant wherein said odorant(s) is capable of interacting with a neuroreceptor in such a way as to have an agonistic effect in order to cause the emission of neurotransmitters which cause and effect to the central nervous system, said effect being a physiological effect which causes the amelioration of female sexual disorder, and particularly the amelioration of HSDD.

According to a ninth aspect of the present invention, there is provided a dopaminergic agonist(s) in the form of at least one dopamine mimetic odorant, wherein said odorant(s) is capable of causing a physiological effect in or from the human brain to cause the amelioration of female sexual disorder, and particularly the amelioration of HSDD.

According to a tenth aspect of the present invention, there is provided a natural human odorant comprising at least one dopamine mimetic odorant(s) and/or a synthetic human odorant comprising at least one dopamine mimetic odorant(s) either or both of which are capable of causing a physiological effect in or from the human brain which causes the amelioration of female sexual dysfunction, and particularly the amelioration of HSDD.

According to an eleventh aspect of the present invention, there is provided a medicament in the form of an aroma comprising at least one dopamine mimetic odorant(s) wherein said aroma has been masked or disguised such that the at least one dopamine mimetic odorant(s) contained therein is not immediately apparent on application to the patient, yet capable of causing a physiological effect in or from the human brain which causes the amelioration of female sexual disorder, and particularly the amelioration of HSDD.

According to a twelfth aspect of the present invention, there is provided an aroma which has a pre-determined character as defined by an electronic nose comprising at least one dopamine mimetic odorant, wherein said aroma is capable of causing a physiological effect in or from the human brain which causes the amelioration of female sexual dysfunction, and particularly the amelioration of HSDD.

The at least one dopamine mimetic odorant may be provided in a suitable solution, such as ethanol, in a concentration up to 40% by volume. Ideally, the concentration is up to 20% by

volume. The concentration of the at least one dopamine mimetic odorant can vary depending upon which DMO or DMOs are being used and the delivery means employed.

The aforementioned aspects of the present invention describe the DMOs of the present invention. The aspects of the invention mentioned hereinafter describe the delivery systems of the present invention for administration of the DMOs to a patient.

According to a thirteenth aspect of the present invention, there is provided a delivery system for any of the at least one dopamine mimetic odorant of the present invention to the patient in the form of a nasal spray. The nasal spray may be administered to the patient by a medical practitioner or by the patient themselves. The at least one dopamine mimetic odorant may be present in as a fluid in an appropriate concentration to be administered to the patient by the form of said nasal spray. Said nasal spray can comprise a reservoir in operative connection with a pump action spray nozzle. The fluid can be housed in a reservoir of the nasal spray until it is to be administered to a patient. It is preferably envisaged that the nasal spray will be placed in or near the nasal cavity/cavities of the patient to facilitate administration of the at least one dopamine mimetic odorant.

According to a fourteenth aspect of the present invention, there is provided delivery system in the form of a patch which is to be worn by the patient which is coated or impregnated with the at least one dopamine mimetic odorant. Typically, the patch is adhered to the skin of the patient to allow the at least one dopamine mimetic odorant to be emitted therefrom and into the patient via their nasal cavities. Such patches are available from The Aromacology Patch Company.

Alternatively, the patch or a strip of patch material may be housed in a protective sheath, such as a plastic sheath, to allow the insertion of same into the nasal cavities of the patient, such that the patient may draw the active ingredient of the present invention into their nasal cavities via an inhalation of breath through their nasal cavities. It is to be appreciated that the appropriate concentrations of the at least one dopamine mimetic odorant are to be used in the patch delivery system and may be included with any other suitable agent to facilitate the release of said at least one dopamine mimetic odorant into the nasal cavity/cavities of the patient.

According to a fifteenth aspect of the present invention, there is provided a delivery system for the at least one dopamine mimetic odorant of the present invention which may be applied topically to the patient for inhalation via the nasal cavities of the patient. Such topical applications could be provided in the form of a lipstick or perfume or any other suitable means which are to be applied to the skin and which are capable of being inhaled by the patient via their nasal cavities.

In order to allow the present invention to be more readily understood embodiments are described below by way of example.

The most preferred DMOs of the present invention comprise at least one of the following: ethyl vanillin (3-ethoxy-4-hydroxybenzaldehyde); isoeugenol (2-methodoxy-4-(1-propenyl) phenol; the woody musk 6,7-dihydro-1,1,2,3,3-pentamethyl-4(5H)-indanone. In order to determine their effectiveness against non-DMOs, a series of formulations were prepared for testing against a series of standardised control formulations.

The DMO formulations comprised (all in ethanol solution to 100% by volume):

1. 20 % Ethyl vanillin (EV)
2. 20 % Ethyl vanillin (EV) and Isoeugenol (4:1 ratio)
3. 20% Ethyl vanillin (EV) and Isoeugenol and woody musk 6,7-dihydro-1,1,2,3,3-pentamethyl-4(5H)-indanone
4. 20% woody musk 6,7-dihydro-1,1,2,3,3-pentamethyl-4(5H)-indanone

The standardised control formulations comprised (all in ethanol solution to 100% by volume):

5. Natural animal cologne
6. Strong carnation natural perfume
7. Intensely sweet fruity perfume

The formulations were applied to separate strips of material and the testers were requested to grade each odour produced on a five-point scale (A-E). The A end of the spectrum denoting

"Like very much/including arousal" and E at the other end of the spectrum "Do not like very much".

Before the experimentation it was hypothesised that the standardised control formulations would produce the following response

5. Natural animal cologne would produce a significant negative response, mainly E and D responses.
6. Strong carnation natural perfume would produce a response roughly in the middle of the spectrum, mainly C responses.
7. Intensely sweet fruity perfume would produce a significant negative response, mainly E and D responses.

Results

The following represent the % of testers grading the odour is marked.

1. Majority A or B
2. Majority A or B
3. Majority B or C
4. Majority A
5. Majority C, D or E
6. Majority B, C or D
7. Majority E

Due to numerous inherent limitations in performing tests of this nature, one such limitation being adaptation when forced to test numerous odours in a short space of time, as well as other well known limitations, it is interesting to note that the testers graded the standardised control formulations (5-8) as expected. More interesting however, is that the formulations of the present invention (1-4) all obtained a majority of the A end of the spectrum, denoting "Like very much/including arousal".

Of course numerous modifications and variations are envisaged with the formulations, compounds, aromas, medicaments or dopamenic agonists of the present invention and these will be apparent to the skilled person without need to depart from the invention.

Claims

1. A dopamine mimetic odorant(s) wherein said odorant(s) causes a physiological effect in, or from, the human brain which ameliorates female sexual dysfunction.

2. A dopamine mimetic odorant(s) as claimed in claims 1, wherein said dopamine mimetic odorant(s) comprises at least one of: vanillin; isoeugenol; and a compound in the woody musk category.

3. A dopamine mimetic odorant(s) as claimed in claims 1 or 2, wherein said dopamine mimetic odorant possesses an appropriate molecular size and electrical charge to interact with a neuroreceptor in the human brain.

4. A dopamine mimetic odorant(s) as claimed in any preceding claim, wherein said dopamine mimetic odorant causes an agonistic effect with neuroreceptors in the human brain to effect the emission of neurotransmitters.

5. A dopamine mimetic odorant(s) as claimed in any preceding claim, wherein said dopamine mimetic odorant is a dopaminergic agonist.

6. A dopamine mimetic odorant(s) as claimed in any preceding claim, wherein said dopamine mimetic odorant(s) comprises at least one of: ethyl vanillin (3-ethoxy-4-hydroxybenzaldehyde); isoeugenol (2-methodoxy-4-(1-propenyl) phenol; and the woody musk 6,7-dihydro-1,1,2,3,3-pentamethyl-4(5H)-indanone.

7. A dopamine mimetic odorant(s) as claimed in any preceding claim, wherein said dopamine mimetic odorant(s) is provided in the concentration of:

- 0-40% (by volume) 3-ethoxy-4-hydroxybenzaldehyde;
- 0-40% (by volume) 2-methoxy-4-(1-propenyl) phenol
- 0-40% (by volume) 6,7-dihydro-1,1,2,3,3-pentamethyl-4(5H)-indanone.

8. A dopamine mimetic odorant(s) as claimed in any one of claims 1-6, wherein said dopamine mimetic odorant(s) is provided in the concentration of:

- 0-20% (by volume) 3-ethoxy-4-hydroxybenzaldehyde;
- 0-20% (by volume) 2- methoxy -4-(1-propenyl) phenol
- 0-20% (by volume) 6,7-dihydro-1,1,2,3,3-pentamethyl-4(5H)-indanone.

9. A dopamine mimetic odorant(s) as claimed in any one of claims 1-6, wherein said dopamine mimetic odorant(s) is provided in the concentration of:

- 1-19% (by volume) 3-ethoxy-4-hydroxybenzaldehyde;
- 0-5% (by volume) 2- methoxy -4-(1-propenyl) phenol
- 1-19% (by volume) 6,7-dihydro-1,1,2,3,3-pentamethyl-4(5H)-indanone

10. An aroma comprising at least one dopamine mimetic odorant as claimed in any preceding claim, wherein said odorant(s) causes a physiological effect in, or from, the human brain which ameliorates female sexual dysfunction.

11. A formulation comprising at least one dopamine mimetic odorant as claimed in any one of claims 1-9, wherein said odorant(s) causes a physiological effect in, or from, the human brain which ameliorates female sexual dysfunction.

12. A medicament comprising at least one dopamine mimetic odorant as claimed in any one of claims 1-9, wherein said odorant(s) causes a physiological effect in, or from, the human brain which ameliorates female sexual dysfunction.

13. A medicament as claimed in claim 12, wherein said medicament is for administration to a patient in avoidance of the human blood brain barrier.

14. A method of ameliorating female sexual dysfunction, whereby said method comprises administering to the olfactory system of a human an effective amount of at least one dopamine mimetic odorant as claimed in any one of claims 1-9.

15. A method as claimed in claim 14, wherein the administration is to the olfactory system of a human in avoidance of the human blood brain barrier.

16. A method of delivery of at least one dopamine mimetic odorant as claimed in any one of claims 1-9, whereby said delivery is facilitated by nasal spray, said dopamine mimetic odorant being housed in a reservoir of said nasal spray which is in operative communication with a spray nozzle of said nasal spray.

17. A method of delivery of at least one dopamine mimetic odorant as claimed in any one of claims 1-9, whereby said delivery is facilitated by a patch worn adjacent to a users skin, said patch being coated or impregnated with the dopamine mimetic odorant.

18. A method of delivery of at least one dopamine mimetic odorant as claimed in any one of claims 1-9, whereby said delivery is facilitated by a strip of material housed in a protective sheath, wherein said strip of material is coated or impregnated with the dopamine mimetic

odorant and at least a proportion of said sheath is open to allow the dopamine mimetic odorant to be released therefrom.

19. The method of claim 19, wherein the protective sheath is provided with suitable closure means to control the release of the dopamine mimetic odorant from the sheath.

INTERNATIONAL SEARCH REPORT

Interna d Application No
PCT/GB 03/00843

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K31/085 A61K31/122 A61K31/115 A61P15/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
PAJ, EPO-Internal, WPI Data, MEDLINE, EMBASE, BIOSIS, SCISEARCH, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 66909 A (HEATON JEREMY P W ;UNIV KINGSTON (CA); ADAMS MICHAEL A (CA)) 29 December 1999 (1999-12-29) page 8, line 8 -page 9, line 9 page 14, line 6-8 page 18, line 13-16; claims 1-3 ---	1,3-5, 11-16
X	GB 2 354 771 A (MCBRIDE ROBERT LTD) 4 April 2001 (2001-04-04) table 1 ---	1-8,10, 11
P,X	EP 1 228 769 A (SCHUER JOERG-PETER PROF) 7 August 2002 (2002-08-07) page 7, line 15,31 page 10, line 44 ---	1-6, 11-13

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
18 June 2003	30/06/2003

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Friederich, M

INTERNATIONAL SEARCH REPORT

Internat	l Application No
	PCT/GB 03/00843

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 02 098966 A (DROM FRAGRANCES INTERNAT KG ;MAIER HANS (DE); MELLER GERHARD (DE)) 12 December 2002 (2002-12-12) tables 1,3	1-8,10, 11

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 03/00843

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: –
because they relate to subject matter not required to be searched by this Authority, namely:

see FURTHER INFORMATION sheet PCT/ISA/210

2. [X] Claims Nos.: –
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 14-19 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box I.1

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

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Continuation of Box I.2

Present claims 1, 2, 10-19 relate to an extremely large number of possible compounds ("dopamine mimetic odorants", "compound in the woody musk category"). In fact, the claims contain so many options that a lack of clarity (and/or conciseness) within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible.

Present claims 3-5, 13, 15 relate to a product/compound defined by reference to a desirable characteristic or property, namely "appropriate molecular size and electrical charge to interact with a neuroreceptor in the human brain", "causes an agonistic effect with neuroreceptors in the human brain to effect the emission of neurotransmitters", "in avoidance of the human blood brain barrier".

The claims cover all products/compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such products/compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the product/compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the products/compounds specifically claimed in the appropriate claims 6-9 and used in the appropriate examples.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Internat Application No
PCT/GB 03/00843

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 9966909	A	29-12-1999	AU	4254799 A	10-01-2000
			CA	2334550 A1	29-12-1999
			WO	9966909 A2	29-12-1999
			EP	1089736 A2	11-04-2001
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			US	2002193442 A1	19-12-2002
			US	2002165122 A1	07-11-2002
			US	6395744 B1	28-05-2002
GB 2354771	A	04-04-2001	NONE		
EP 1228769	A	07-08-2002	EP	1228769 A1	07-08-2002
			WO	02067986 A2	06-09-2002
WO 02098966	A	12-12-2002	WO	02098966 A2	12-12-2002